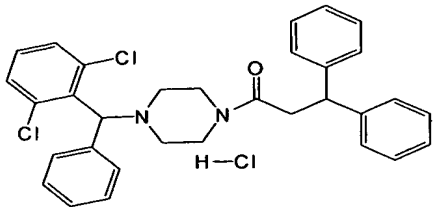
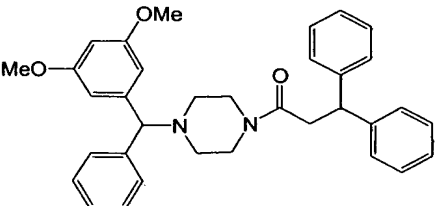
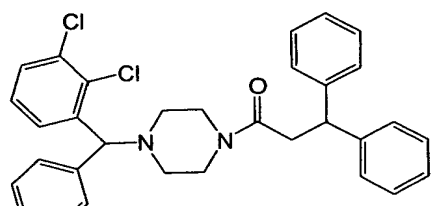
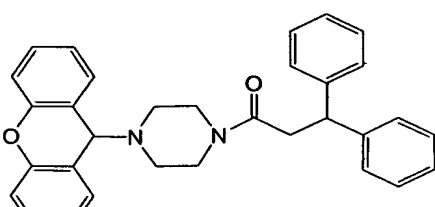
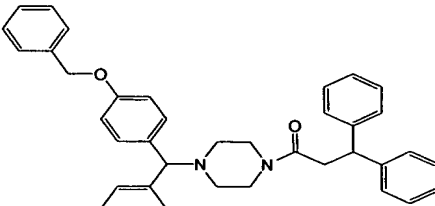
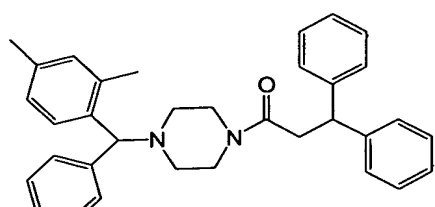


| Compound | Name  | Structure |
|----------|---|-----------|
| P1       | 3,3-Diphenyl-1-{4-[phenyl-(4-trifluoromethyl-phenyl)-methyl]-piperazin-1-yl}-propan-1-one             |           |
| P2       | 3,3-Diphenyl-1-{4-[phenyl-(3-trifluoromethyl-phenyl)-methyl]-piperazin-1-yl}-propan-1-one             |           |
| P3       | 1-{4-[(4-Methoxy-phenyl)-(4-trifluoromethyl-phenyl)-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one |           |
| P4       | 1-{4-[(3,5-Di-tert-butyl-4-hydroxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one   |           |
| P5       | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid ethyl ester                      |           |
| P6       | 1-{4-[(4-Chloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one                      |           |

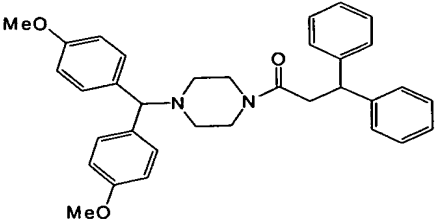
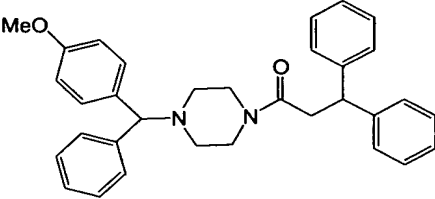
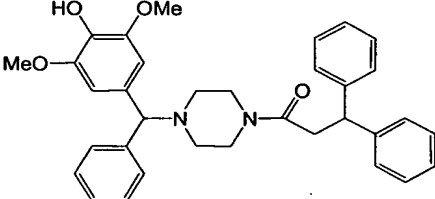
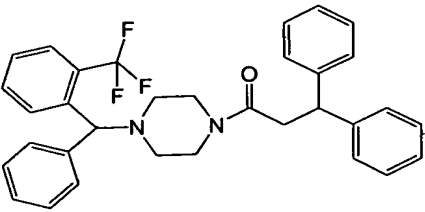
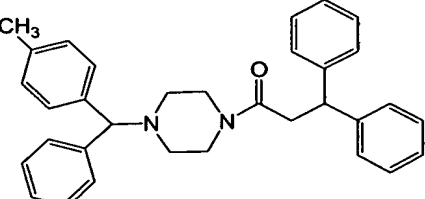
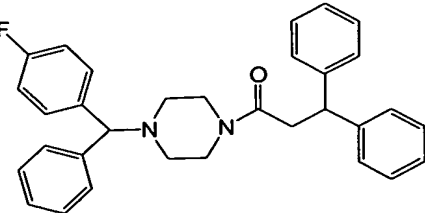
**Figure 1**

| Compound | Name  | Structure |
|----------|---|-----------|
| P7       | 1-[4-(Benzo[1,3]dioxol-5-yl-phenyl-methyl)-piperazin-1-yl]-3,3-diphenyl-propan-1-one            |           |
| P8       | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid                            |           |
| P9       | 1-{4-[(3,5-Dichloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one            |           |
| P10      | 1-{4-[(3,5-Bis-trifluoromethyl-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one |           |
| P11      | 1-{4-[(4-tert-Butyl-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one            |           |
| P12      | 1-{4-[(2-Difluoromethoxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one       |           |

**Figure 1**

| Com-<br>pound | Name  | Structure  |
|---------------|---|--|
| P13           | 1-{4-[(2,6-Dichloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one  |    |
| P14           | 1-{4-[(3,5-Dimethoxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one |    |
| P15           | 1-{4-[(2,3-Dichloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one  |    |
| P16           | 3,3-Diphenyl-1-[4-(9H-xanthen-9-yl)-piperazin-1-yl]-propan-1-one                      |  |
| P17           | 1-{4-[(4-Benzyloxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one   |  |
| P18           | 1-{4-[(2,4-Dimethyl-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one  |  |

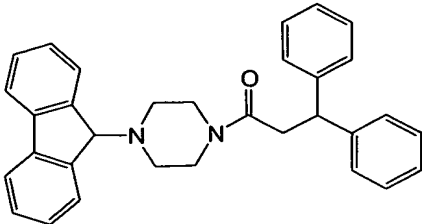
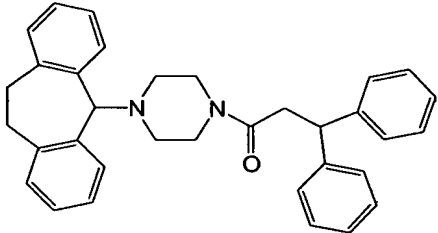
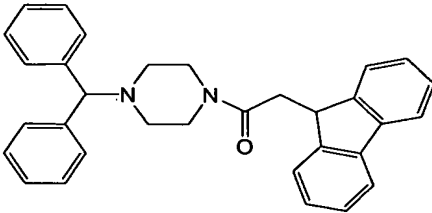
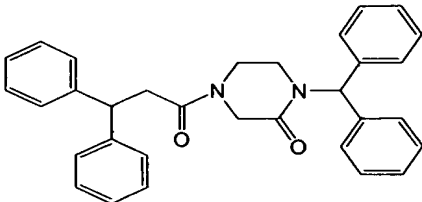
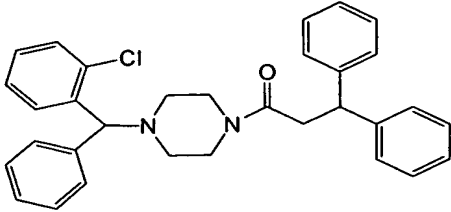
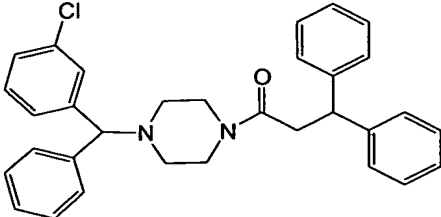
**Figure 1**

| Compound | Name  | Structure  |
|----------|---|--|
| P19      | 1-{4-[Bis-(4-methoxy-phenyl)-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one                  |    |
| P20      | 1-{4-[(4-Methoxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one               |    |
| P21      | 1-{4-[(4-Hydroxy-3,5-dimethoxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one |   |
| P22      | 3,3-Diphenyl-1-{4-[phenyl-(2-trifluoromethyl-phenyl)-methyl]-piperazin-1-yl}-propan-1-one       |  |
| P23      | 3,3-Diphenyl-1-[4-(phenyl-p-tolyl-methyl)-piperazin-1-yl]-propan-1-one                          |  |
| P24      | 1-{4-[(4-Fluoro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one                |  |

**Figure 1**

| Compound | Name  | Structure |
|----------|---|-----------|
| P25      | 3,3-Diphenyl-1-{4-[phenyl-(3,4,5-trimethoxy-phenyl)-methyl]-piperazin-1-yl}-propan-1-one              |           |
| P26      | 1-{4-[Benzo[1,3]dioxol-5-yl-(4-methoxy-phenyl)-methyl]-piperazin-1-yl}-3,3-diphenylpropan-1-one       |           |
| P27      | 1-[4-(10,10-Dioxo-9,10-dihydro-10lambda*6*-thioxanthen-9-yl)-piperazin-1-yl]-3,3-diphenylpropan-1-one |           |
| P28      | 3,3-Diphenyl-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-propan-1-one                                  |           |
| P29      | 1-{4-[(2,4-Dichloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenylpropan-1-one                   |           |
| P30      | 1-{4-[(3,4-Dichloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenylpropan-1-one                   |           |

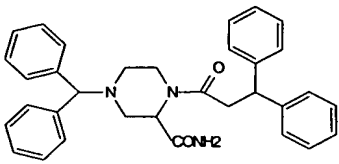
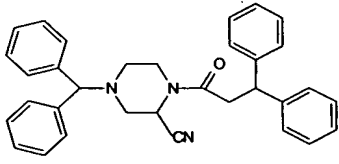
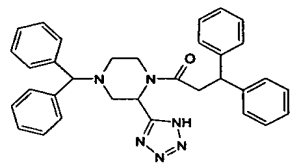
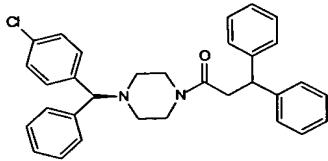
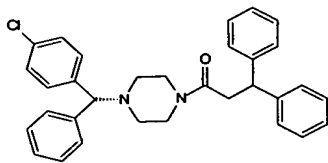
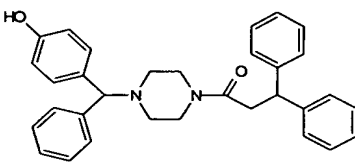
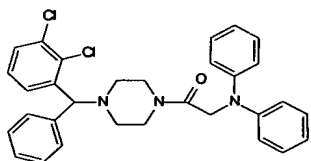
**Figure 1**

| Compound | Name   | Structure  |
|----------|--|--|
| P31      | 1-[4-(9H-Fluoren-9-yl)-piperazin-1-yl]-3,3-diphenyl-propan-1-one                               |    |
| P32      | 1-[4-(10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-piperazin-1-yl]-3,3-diphenyl-propan-1-one |    |
| P33      | 1-(4-Benzhydryl-piperazin-1-yl)-2-(9H-fluoren-9-yl)-ethanone                                   |   |
| P34      | 1-Benzhydryl-4-(3,3-diphenyl-propionyl)-piperazin-2-one  |  |
| P35      | 1-{4-[(2-Chloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one               |  |
| P36      | 1-{4-[(3-Chloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one               |  |

**Figure 1**

| Compound | Name   | Structure |
|----------|--|-----------|
| P37      | 1-(4-Benzhydryl-2-methyl-piperazin-1-yl)-3,3-diphenyl-propan-1-one                 |           |
| P38      | 4-Benzhydryl-1-(2-9H-fluoren-9-yl-acetyl)-piperazine-2-carboxylic acid             |           |
| P39      | 4-Benzhydryl-1-(2-9H-fluoren-9-yl-acetyl)-piperazine-2-carboxylic acid ethyl ester |           |
| P40      | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid               |           |
| P41      | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid ethyl ester   |           |
| P42      | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid               |           |
| P43      | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid ethyl ester   |           |

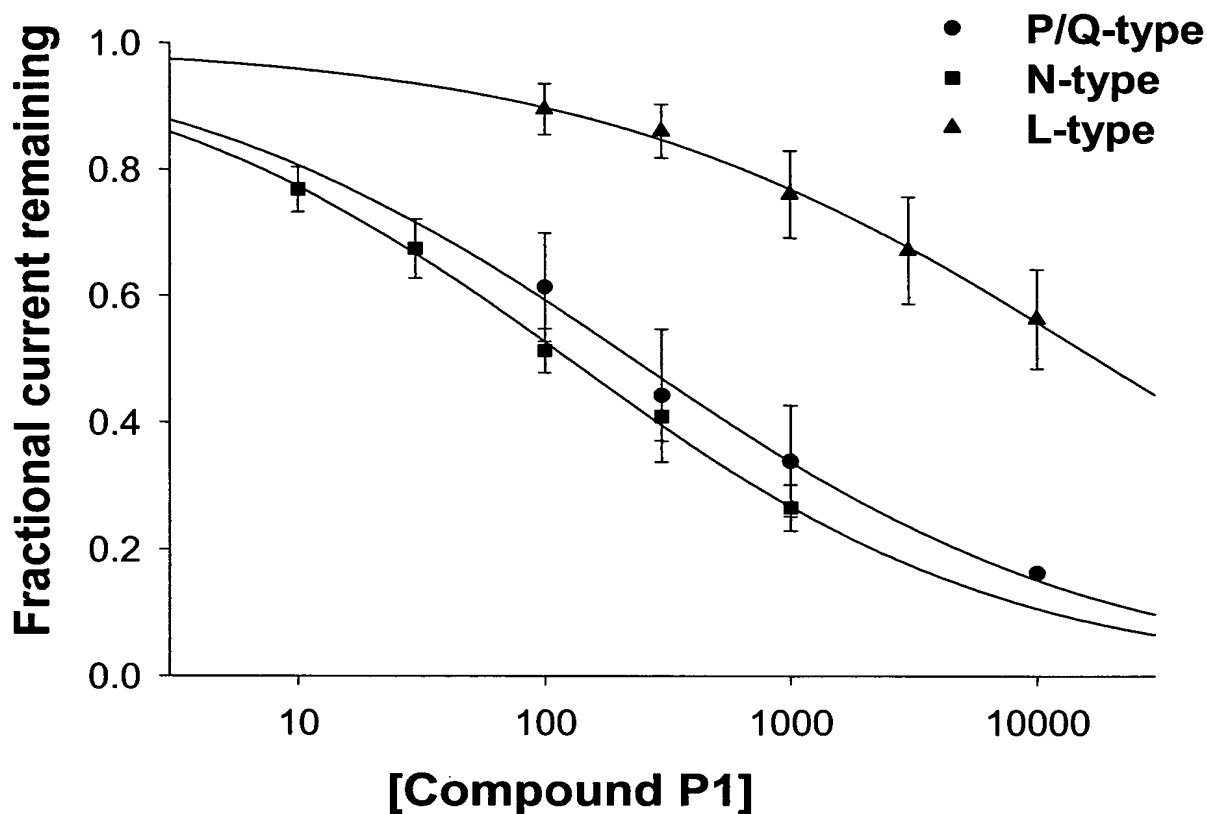
**Figure 1**

| Compound | Name  | Structure  |
|----------|---|--|
| P44      | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carboxylic acid amide          |    |
| P45      | 4-Benzhydryl-1-(3,3-diphenyl-propionyl)-piperazine-2-carbonitrile                   |    |
| P46      | 1-[4-Benzhydryl-2-(1H-tetrazol-5-yl)-piperazin-1-yl]-3,3-diphenyl-propan-1-one      |    |
| P47      | 1-{4-[(4-Chloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one    |   |
| P48      | 1-{4-[(4-Chloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one    |  |
| P49      | 1-{4-[(4-Hydroxy-phenyl)-phenyl-methyl]-piperazin-1-yl}-3,3-diphenyl-propan-1-one   |  |
| P50      | 1-{4-[(2,3-Dichloro-phenyl)-phenyl-methyl]-piperazin-1-yl}-2-diphenylamino-ethanone |  |

**Figure 1**



Selectivity of Compound P1 for N-type  $\text{Ca}^{2+}$  Channels



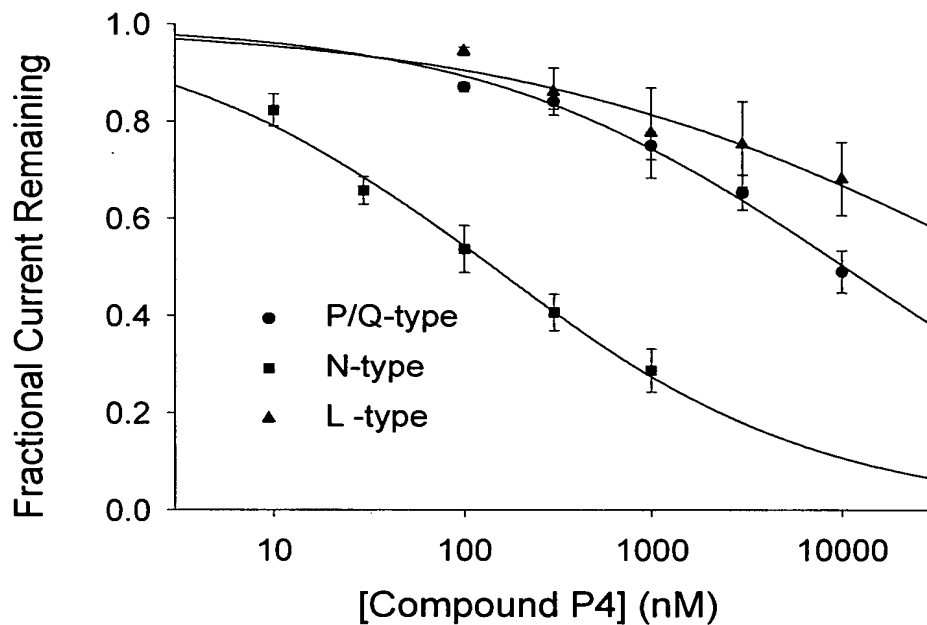
P/Q-type  $\text{IC}_{50} = 966 \pm 461 \text{ nM}$  ( $n=7$ )

N-type  $\text{IC}_{50} = 190 \pm 70 \text{ nM}$  ( $n=10$ )

L-type  $\text{IC}_{50} \gg 10 \text{ }\mu\text{M}$  (estimated:  $19.6 \pm 9.2 \text{ }\mu\text{M}$ ) ( $n=5$ )

**Figure 2**

### Effect of Compound P4 on Various $\text{Ca}^{2+}$ Channels



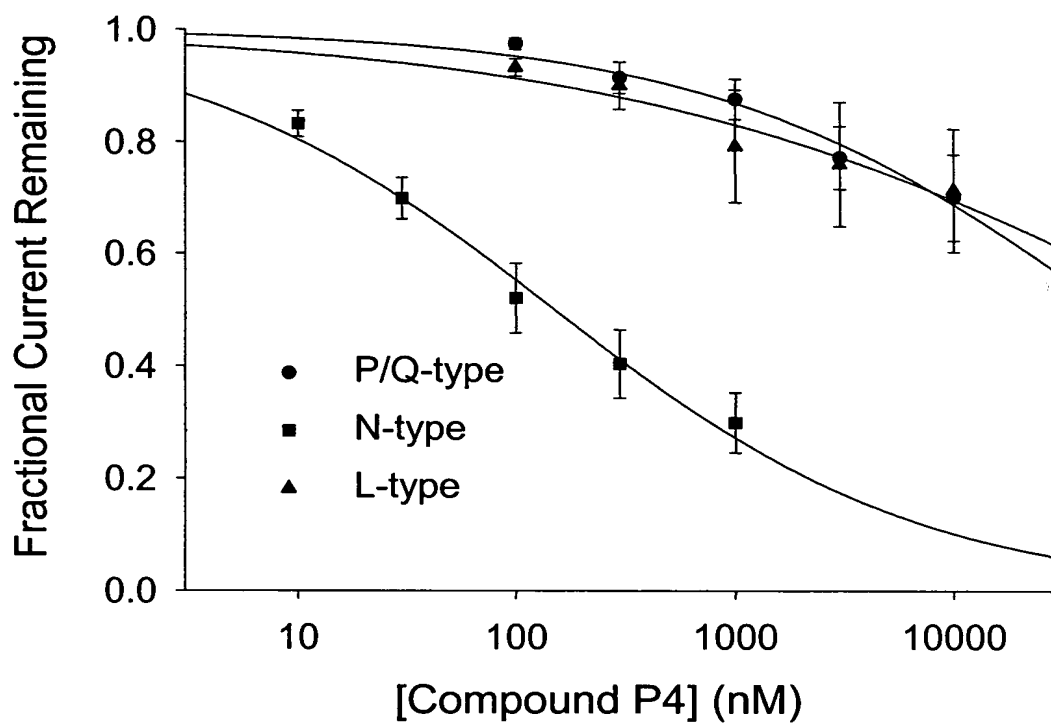
$\text{IC}_{50}$  P/Q-type =  $7592 \pm 1076$  nM (n=4)

$\text{IC}_{50}$  N-type =  $185 \pm 68$  nM (n=5)

$\text{IC}_{50}$  L-type  $\gg 10$   $\mu\text{M}$  (n=5)

**Figure 3**

### Effect of Compound P4 on Various $\text{Ca}^{2+}$ Channels



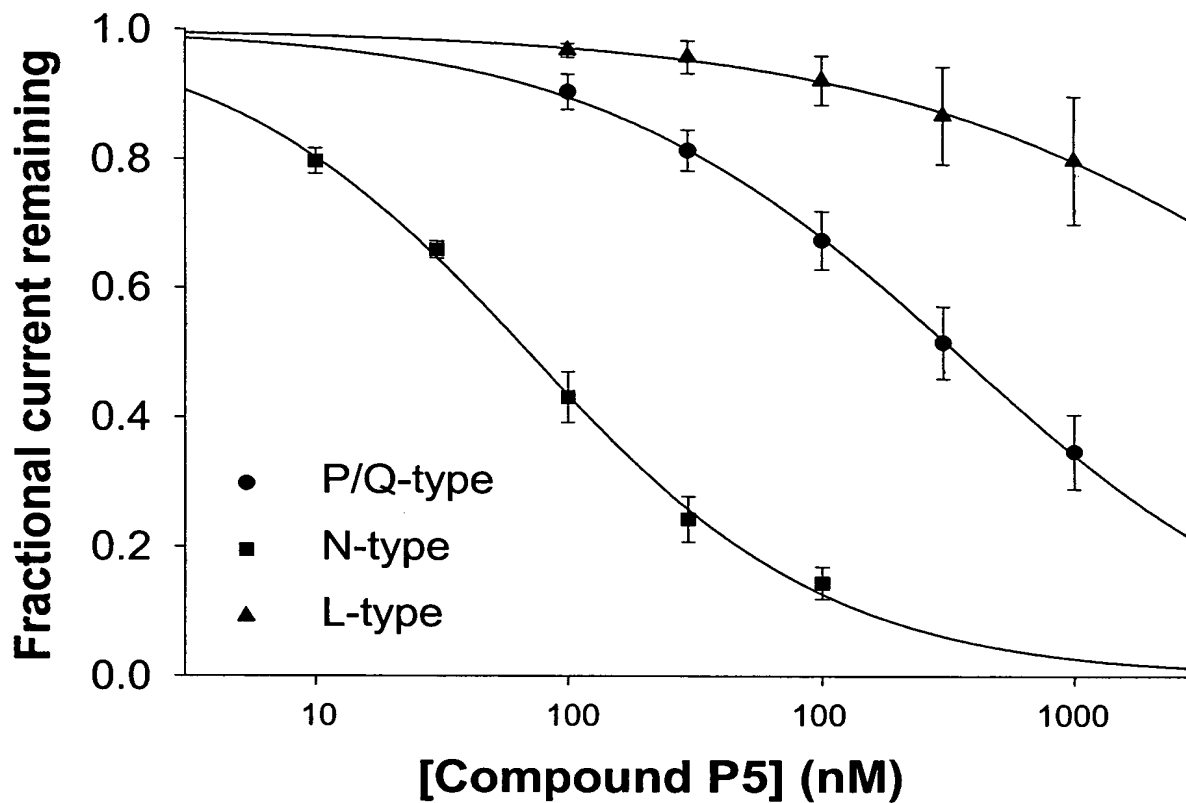
$\text{IC}_{50}$  P/Q-type  $\gg 10 \mu\text{M}$  (n=5)

$\text{IC}_{50}$  N-type =  $251 \pm 103 \text{ nM}$  (n=6)

$\text{IC}_{50}$  L-type  $\gg 10 \mu\text{M}$  (n=5)

**Figure 4**

Selectivity of Compound P5 for N-type  $\text{Ca}^{2+}$  Channels



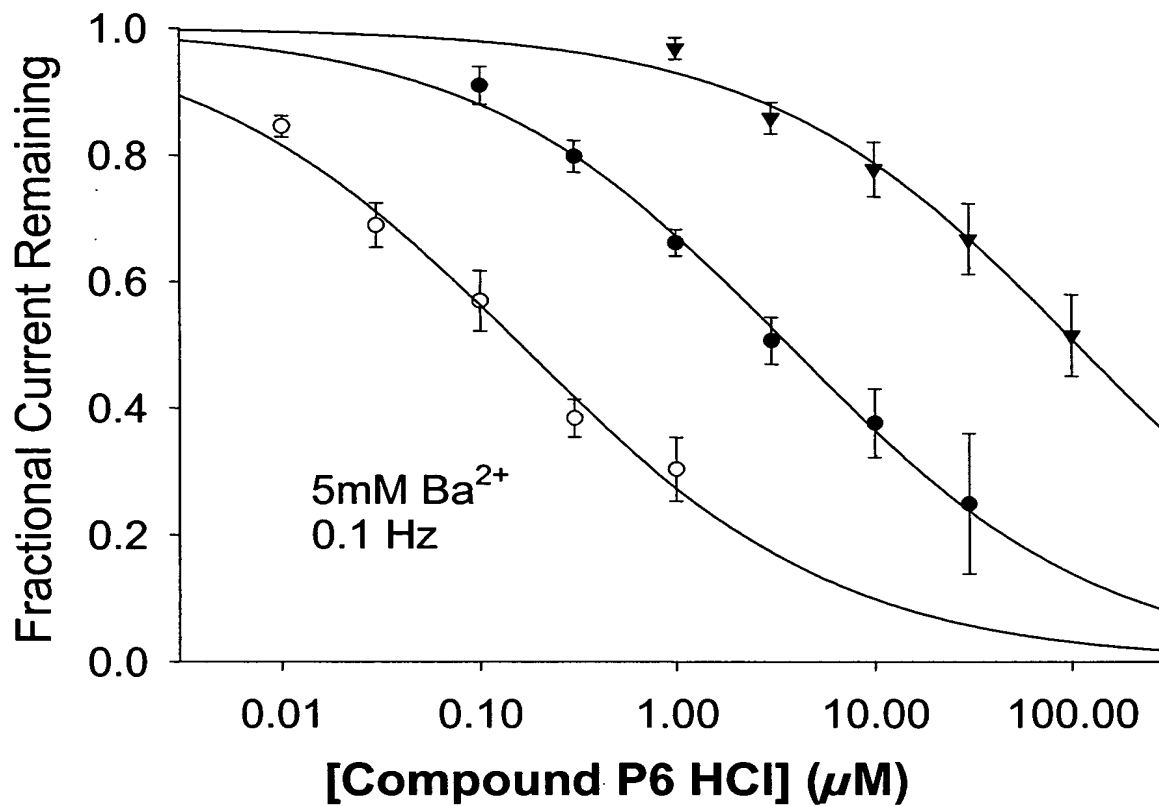
P/Q-type  $\text{IC}_{50} = 5.028 \pm 1.979 \mu\text{M}$  (n=6)

N-type  $\text{IC}_{50} = 0.073 \pm 0.01 \mu\text{M}$  (n=5)

L-type  $\text{IC}_{50} = 210 \pm 130 \mu\text{M}$  (n=6)

**Figure 5**

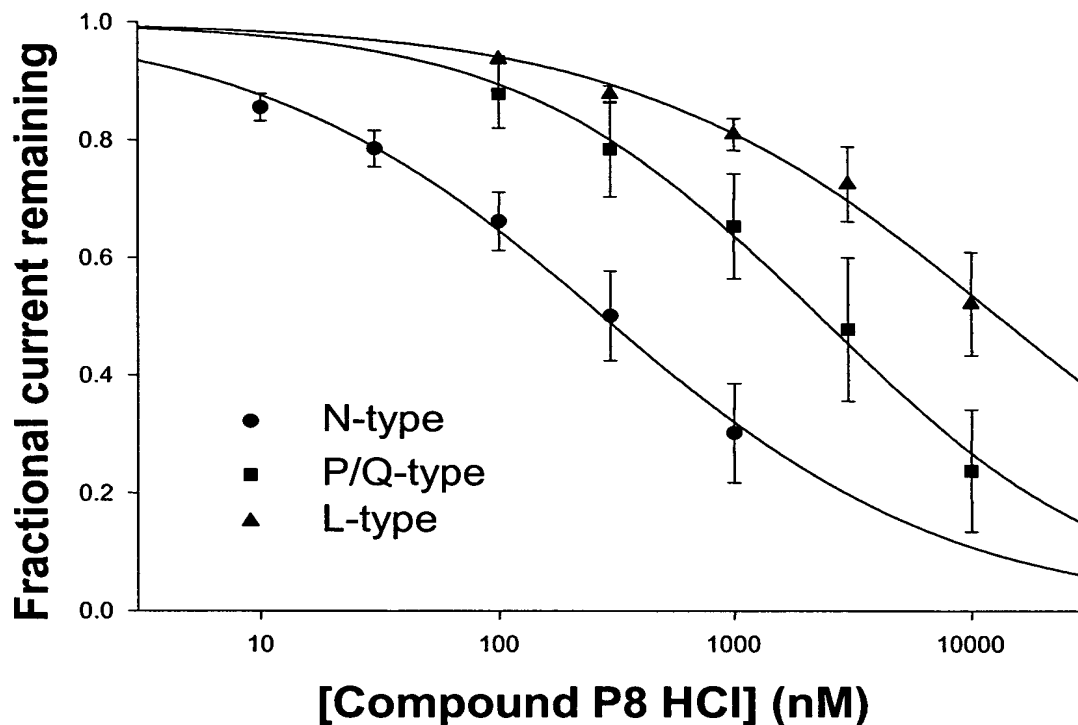
Selectivity of Compound P6 for N-type  $\text{Ca}^{2+}$  Channels



- P/Q-type  $\text{IC}_{50} = 4.5 \pm 1.3 \mu\text{M}$  (n=5)
- N-type  $\text{IC}_{50} = 0.16 \pm 0.03 \mu\text{M}$  (n=5)
- ▼ L-type  $\text{IC}_{50} = 133 \pm 50 \mu\text{M}$  (n=6)

**Figure 6**

Selectivity of Compound P8 for N-type  $\text{Ca}^{2+}$  Channels



P/Q-type  $\text{IC}_{50} = 3.383 \pm 1.455 \mu\text{M}$  (n=5)  
N-type  $\text{IC}_{50} = 0.359 \pm 0.135 \mu\text{M}$  (n=5)  
L-type  $\text{IC}_{50} = 37.140 \pm 20.930 \mu\text{M}$  (n=5)

**Figure 7**